REMARKS/ARGUMENTS

Claims 24, 27-34, 39, 41-44, 48-51, 53-54, and 58 are under examination in this case. Claims 1-22 had previously been canceled. Claims 25-26, 35-38, and 40 have been canceled without prejudice and claims 45-47, 52, and 55-57 have been withdrawn as non-elected claims in the present Amendment. Claim 23 has been canceled without prejudice and replaced with new claim 58. Claims 24, 27-34, 39, 41-44, 48-51, and 53 have been amended for improved clarity and proper dependency. The Specification has been amended to correct a typographical error in the Abstract. No new matter has been added with this Amendment.

Election/Restrictions:

Applicants acknowledge the finality of the Restriction Requirement. Accordingly, claims 45-47, 52 and 55-57 have been withdrawn as non-elected claims. Applicants reserve the right to file one or more divisional or continuation applications to pursue the subject matter of non-elected claims.

Claim Rejections under 35 U.S.C. 102:

Claims 23-34, 41-44 and 53 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Reiter et al. (Nuc. Acid. Res 1996 24: 4050-4056). Claims 23-36, 41-44 and 53 are further rejected under 35 U.S.C. 102(b) as allegedly anticipated by Maihle et al. (PNAS 1991 88:1825-1829). Applicants respectfully traverse these rejections.

The Office Action alleges that Reiter et al. teaches human EGFR, ErbB1-S that contains the first two domains and part of the third and that the ligand binding properties are an inherent feature of this protein. Mahle et al. is alleged to teach a truncated avian c-ErbB that contains all of the first three domains and the first two amino acids of the fourth and that the ligand binding properties are inherent to the protein.

Without acquiescing to these allegations and in the interest of advancing prosecution of this application, the claims at issue have been amended. Applicants submit that the amended claims are not anticipated by the cited art for the following reasons.

Reiter *et. al.* describes a truncated ErbB1 extracellular domain that comprises residues 1 to 357 (after the signal peptide is removed during secretion). Such a construct lacks most of the residues in the L2 domain that are required for high affinity binding to EGFR ligands. Similarly, the truncated ectodomain described in Maihle *et. al.* lacks the entire L2 domain. Again, this truncated ectodomain is unlikely to bind EGFR ligands.

Neither of the cited references teaches the truncated ectodomain comprising at least residues 1 to 492 of ErbB1 which shows increased binding affinity for at least one ErbB1 ligand when compared to the full length ectodomain. The Examiner contends that ligand binding properties are inherent to the truncated ectodomains described in these citations. Applicants disagree. Applicants emphasize that the truncated ErbB1 ectodomain claimed herein has an <u>increased</u> binding affinity for EGF ligands. Nothing in the cited references teaches the claimed invention. Applicants further argue that there is no extrinsic evidence to support a finding of inherency as alleged by the Examiner. See *In Continental Can Company USA, Inc vs Monstanto Co.* 948 F.2d 1264, 1268, 20 USPQ2d 1746 (Fed. Cir. 1991):

> "To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is *necessarily* present in the thing described in the reference, and that that it would be so recognized by persons of ordinary skill. (*Emphasis added.*)

As noted above, it is known in the art that the L2 domain of EGFR molecules is important in ligand binding. Thus, it cannot be said that the truncated ectodomains disclosed in the references inherently possess ligand

binding properties, and it has not been shown in either reference that the relevant ectodomain necessarily binds to an ErbB1 ligand. Further, neither reference provides a method for determining whether the truncated ectodomain demonstrates increased binding affinity for at least one ErbB1 ligand when compared to the full length ectodomain. The courts have given repeated reminders as to the improper use of the inherency in rejecting claims:

> "Inherency, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient. See Parker v. Ballantine, 26, C.C.P.A. 799, 101 F.2d 220 (Patent Appeal No. 4026, decided January 1939); In re Ball, 23 C.C.P.A. 1053, 96 F.2d 301. If however, the disclosure is sufficient to show that the natural result flowing from the operation *as taught* would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient. *In Hansgirg v. Kemmer,* 26 C.C.P.A. 937, 940, 102 F.2d 212, 214, 40 USPQ 665, 667 (1939)). (*Emphasis added.*)

Based on the above, Applicants argue that the truncated ErbB1 with increased binding affinity as claimed is not taught by the cited references nor inherent in the teachings of either of these citations.

Claim Rejections under 35 U.S.C. 103:

Claims 48-51 and 54 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Reter et al. or Maihle et al. in view of Ashkenazi et al. (Current Opinions in Immunology 1997 9:195-200). Applicants respectfully traverse this rejection.

The shortcomings of Reter et al. and Maihle et al. have been discussed above. Ashkenazi et al. is a general reference which describes the use of immunoadhesins as research tools and therapeutic agents. A rejection for obviousness over a combination of references cannot be sustained unless some motivation to combine the teachings therein can be found within the references themselves. In *re Lee*, 61 USPQ 2d 1430

(Fed. Cir. 2002). Neither Reiter et al. nor Maihle et al. provides any motivation to a skilled artisan to combine their teachings with Ashkenazi et al. Nothing in Reiter et al. or Maihle et al. suggests the truncated ErbB1 ectodomains with increased binding affinity.

With the entry of the present Amendment, claims 48-51 specify that the chimeric or fusion constructs comprise the truncated ErbB1 ectodomain defined in the amended claims of 24 and 58. Claim 54 is a dependent claim of amended claim 48. If the truncated ErbB1 ectodomains defined in claims 24 and 58 are considered to be novel and unobvious based on the above arguments, then it follows that any dependent claims comprising such truncated ErbB1 ectodomains should also be novel and unobvious.

Applicants submit that claims 48-51 and 54 as amended are not *prima facie* obvious over Reiter et al. or Maihle et al. in view of Ashkenazi et al.

Claim Rejections under 35 U.S.C. 112:

Claims 23-44, 48-51, 53, and 54 are rejected under 35 U.S.C. 112, first paragraph, on the ground that the Specification allegedly does not reasonably provide enablement for all truncations of all EGFR and EGFR-like proteins and fails to comply with the written description requirement. Applicants respectfully traverse these rejections.

Without acquiescing to this rejection and in the interest of advancing prosecution of this case, the claims have been amended such that these rejections are no longer relevant. Specifically, the claims have been amended to define a specific truncated ErbB1 ectodomain comprising at least residues 1-492 of ErbB1 which show an increased binding affinity. The amended claims therefore clearly recite the structural features of the truncated ErbB1 ectodomain required in order to achieve increased

binding affinity for at least one ErbB1 ligand. The specification also provides methods by which truncated ectodomains can be tested for increased binding affinity to ErbB1 ligands (see the description of BIAcore binding assays at page 14, lines 12 to 23). Accordingly, Applicants submit that the invention as claimed is sufficiently described in the specification in a manner as to enable any person skilled in the art to make and use it.

The Office Action asserts that "applicant has not described the characteristics of this truncation so that one of skill in the art could predictably identify other truncations with the same enhanced affinity." (see page 5, lines 16-18).

Applicants argue that because of the shared structural characteristics of the EGFR family members, any corresponding truncated EGFR molecules in the family made based on the examples provided in the specification are expected to have similar binding properties. As described on page 6 in the Specification, EGFR receptor family members show similar domain arrangements and share significant sequence identify. Thus, a person of ordinary skill in the art can introduce a corresponding truncation in an EGFR (e.g. ErbB2, ErbB3, or ErbB4) to increase the binding affinity of that EGFR for at least one EGFR ligand.

Claims 23-44, 48-51, 53, and 54 are rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite. Applicants respectfully traverse this rejection.

Applicants submit that the meaning of the term "EGFR" is clear to a person of ordinary skill in the art, i.e., a protein which binds specifically and selectively a known EGFR ligand such as EGF. A skilled artisan also understands that the members of the EGFR family show similar domain arrangements and share significant sequence identity. Furthermore, the Specification provides sufficient descriptions of terms such as "domain", "module", or "subdomain" (see pages 1, 2, 6 and 7). Because of the shared

structural characteristics of the EGFR family members, any corresponding truncated EGFR molecules are expected to have the similar binding properties.

However, the claims at issue have been amended to address the issues raised in the Office Action without acquiescing to the rejection and in the interest of advancing prosecution of the present application. Withdrawal of the rejection under 35 U.S.C. 112, second paragraph, is respectfully requested.

Based on the amendments and arguments presented above, Applicants request withdrawal of the rejection under 35 U.S.C. 112.

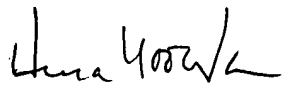
CONCLUSION

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are further issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This amendment is accompanied by a Petition for Extension of Time (two months) and a check in the amount of $420.00 as required under 37 C.F.R. 1.17. It is believed that this amendment does not necessitate the payment of any additional fees under 37 C.F.R. 1.16-1.17. If the amount submitted is incorrect, however, please deduct from Deposit Account No. 07-1969 the appropriate fee for this submission and any extension of time required.

Respectfully submitted,



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